

REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Comments regarding Status of the Application

Initially, Applicants note a few errors in the Status of the Application, provided by the Examiner in the first paragraph of the Office Action. To ensure a complete and accurate record, Applicants provide the following clarification. The previous Office Action was in response to Applicants' arguments filed March 10, 2008. Further, claims 3 and 4 were amended, and claims 3-5 were pending and examined.

Claim Amendments

Claim 3 has been amended to clarify that the method of inhibition of keloid and/or hypertrophic scar formation is in a course of therapy of wound or dermal injury, to delete the salt of acetylsalicylic acid, to recite "treatment" of pain or pruritus, and to make editorial changes. Support for these amendments is set forth on page 2, lines 6-7 of Applicants' specification. Claim 5 has also been amended to be consistent with claim 3.

Claim 4 has been cancelled, without prejudice.

New claims 6 and 7 have been added to the application. Support for these claims is found on page 5, lines 11-14 of Applicants' specification.

No new matter has been added to the application by these amendments.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 3-5 under 35 U.S.C. § 112, first paragraph, as not being fully enabled by the specification, is respectfully traversed for the following reasons.

The Examiner takes the position that the specification is not enabling for the inhibition/prevention of keloid and/ or hypertrophic scar formation, and for inhibition of pain and pruritus.

Initially, claim 3 has been amended to recite "treatment" of pain and pruritus, and claim 4 has been cancelled, thus rendering moot this portion of the rejection.

Further, the remaining claims have been amended to clarify that the method of inhibition is in a course of therapy of wound or dermal injury. Applicants' specification and the data provided therein clearly provide enablement for the claimed methods. Applicants direct the Examiner's attention to the Examples of the specification, in particular Test 1 (page 15, line 15 to page 16, line 9) and Test 5 (page 19, line 10 to page 20, line 8.)

Accordingly, the above rejection should be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 3-5 under 35 U.S.C. 112, second paragraph, as being indefinite is respectfully traversed.

The Examiner takes the position that the term "effective amount" is a relative term that renders the claim indefinite. The Examiner further states that although the specification discloses an effective amount, one is not able to ascertain from the broad range provided, what an effective amount would be to carry forth said invention.

MPEP 2173.05(c) states that "[t]he common phrase 'an effective amount' may or may not be indefinite. The proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure. See *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975)." As admitted by the Examiner, Applicants' specification does provide specific values, e.g., in the Examples.

MPEP 2173.05(c) further states that "[t]he phrase 'an effective amount . . . for growth stimulation' was held to be definite where the amount was not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is. *In re Halleck*, 422 F.2d 911, 164 USPQ 647 (CCPA 1970)." (Emphasis added.)

This section of the MPEP also explains that "[t]he phrase 'an effective amount' has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art. *In re Fredericksen* 213 F.2d 547, 102 USPQ 35 (CCPA 1954)." This is clearly not the situation with Applicants' pending claims, as the claims clearly recite what function is to be achieved.

Lastly, this section of the MPEP states that “[t]he more recent cases have tended to accept a limitation such as ‘an effective amount’ as being definite when read in light of the supporting disclosure and in the absence of any prior art which would give rise to uncertainty about the scope of the claim. In *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an ‘effective amount of a compound of claim 1’ without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected.” (Emphasis added.)

It is thus clear that the term “effective amount” does not render the claims indefinite, particular when read in light of Applicants’ disclosure, and in view of the relevant case law.

Accordingly, Applicants respectfully assert that the above-rejection is untenable and should be withdrawn.

Patentability Arguments

The patentability of the present invention over the disclosure of the reference relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejection Under 35 U.S.C. § 102(b)

The rejection of claims 3-5 under 35 U.S.C. § 102(b) as being anticipated by Cappelli-Schellpfeffer (WO 01/70210) is respectfully traversed.

An object of the present invention is to provide a method for inhibition of keloid and/or hypertrophic scar **formation in a course of therapy of wound of dermal injury**. This is distinct from a method for treatment of a keloid or hypertrophic scar which is already formed.

The Examiner takes the position that Cappelli-Schellpfeffer specifically teaches the topical application of aspirin on the surface of a scar or healed wound, including keloids. The reference provides working examples where topical application of aspirin reveals scar contracture and flattened scar contours. (See Examples 4 and 5 of the reference.)

As explained in detail in the last response, according to Example 4 of Cappelli-Schellpfeffer, a combination of 2% salicylic acid and hydrogel was topically applied to the

patient (see page 30, lines 21-23). The patient had orally received acetylsalicylic acid to prevent thromboembolic post-operative complications (scar, etc.) (See page 30, lines 15-16.) According to Example 5 of Cappelli-Schellpfeffer, a combination of 2% salicylic acid and hydrogel was topically applied to the patient (see page 31, lines 6-8).

The Examiner appears to confuse acetylsalicylic acid (aspirin), as in Applicants' claims, and salicylic acid, as in the reference.

Further, the description on page 11, lines 23-27 of Cappelli-Schellpfeffer is not discussing acetylsalicylic acid.

In view of the above-discussed distinction, Applicants respectfully request that the Examiner reconsider Applicants' previous remarks. For the Examiner's convenience, these comments are restated below, together with additional comments.

Cappelli-Schellpfeffer does not disclose that acetylsalicylic acid is effective for inhibition of keloid and/or hypertrophic scar formation, etc. According to Example 1 of the reference, the combination of nabumetone and diphenhydramine was orally administered to the patient. Hydrogel or a gel was co-administered with the drugs and topically applied as gel sheeting . . . (See page 28, lines 19-24.) According to Example 2, nabumetone was orally administered to the patient. Hydrogel sheeting was topically applied . . . (See page 29, lines 16-19.) According to Example 3, nabumetone was orally administered to the patient. Hydrogel sheeting was topically applied . . . (See page 29, last line to page 30, line 3.) Examples 4 and 5 are explained above.

As explained above, acetylsalicylic acid was never topically administered to the patients in order to treat a scar or a keloid. In the case of topical administration, the effect on a scar was confirmed only on 2% salicylic acid. In case of nabumetone, the effect on a scar, etc. was confirmed only when the drug was orally administered. Surprisingly, in Example 4 of the reference, acetylsalicylic acid (325mg tablet) was already orally administered to prevent thromboembolic post operative complications, before receiving the treatment of salicylic acid.

It is described in the reference that the invention provides for administration of the cyclooxygenase inhibitor that is either a topical or transdermal administration, an oral administration, etc. (See page 12, lines 4-9.) However, with regards to acetylsalicylic acid, the reference reveals that even when this drug is orally administered to the patient suffering from a

scar, etc., it is not effective. Therefore, the description that the cyclooxygenase inhibitor can be used orally or topically contradicts the description of Example 4.

As explained above, there is no working example in the reference in which acetylsalicylic acid is used for inhibiting or treating a scar, etc., by topical administration of the drug to the patient; and there is no data supporting that topical acetylsalicylic acid is effective for treating a scar, etc.

Even if acetylsalicylic acid is a cyclooxygenase inhibitor, it was not confirmed that all cyclooxygenase inhibitors exhibit effectiveness for treating a scar, etc., because only salicylic acid exhibits such an activity in topical application. The notion that (topical) acetylsalicylic acid is effective for treating a scar, etc. is based completely on speculation. Applicants believe that the present invention, completed on the basis of concrete data, should not be denied by the reference disclosure based on speculation.

Further, even assuming for the sake of argument that Cappelli-Schellpfeffer discloses topical application of aspirin on the surface of a scar or healed wound including keloids, the timing for treating the keloid or scar is completely different from that of Applicants' invention. Specifically, Applicants' method is directed to a method of inhibition while the wound and dermal injury is being treated, i.e., when the keloid or scar has not yet formed. On the contrary, Cappelli-Schellpfeffer teaches improving the size and appearance of a healed wound or scar.

As recited in Applicants' claim 3, one object of Applicants' invention is a method for inhibiting the formation of a keloid or scar by topically administering aspirin in a course of therapy of wound or dermal injury. Specifically, by topically administering aspirin to the patient during treatment of the wound or dermal injury, the wound or dermal injury can be inhibited, thus hardly forming a keloid or scar, and without delay of wound healing. (Please see page 2, lines 6-14 of Applicants' specification.)

In Test 1 of Applicants' specification, in a heat wound model test by using type 2 diabetic modeled mice, the excellent effect of acetylsalicylic acid on prevention (inhibition) of the scar contracture on the burn wound after epithelialization is confirmed. (See Table 8.) Furthermore, in Test 2, on inhibition of collagen gel shrinking in vitro, the shrinking of collagen was inhibited in the group containing acetylsalicylic acid. (See Tables 9 and 10.) This data demonstrates that acetylsalicylic acid is effective for inhibition of the formation of a keloid or scar in a course of

therapy of wound or dermal injury. Furthermore, according to Tests 3 and 4, acetylsalicylic acid does not delay the wound healing by the topical administration thereof. (See Tables 11 and 12.)

As explained above, it is shown that acetylsalicylic acid, when it is topically administered in a course of therapy of wound or dermal injury, inhibits the formation of a keloid or scar without delay of wound healing. On the contrary, Cappelli-Schellpfeffer discloses that cyclooxygenase inhibitors are administered to a healed wound or scar formed after treatment of a wound or dermal injury to improve the surface or size thereof.

In the specification of Cappelli-Schellpfeffer, the term “healed wound or scar” is defined on page 6, lines 16-22. It is clear from this definition that the term refers to a scar after being treated. Further, in Examples 1 to 5 of Cappelli-Schellpfeffer, the patients who are treated already have scars. See in particular, Example 3, wherein the patient had an irritated scar on the forearm for more than 2 years.

Thus, it is clear that the subject matter of Applicants’ claims is clearly patentable over the teachings of Cappelli-Schellpfeffer. Accordingly, the above rejection is untenable and should be withdrawn.

Conclusion

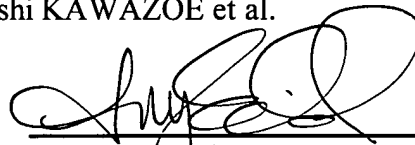
Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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